REMARKS

The above amendments to the above-captioned application along with the following remarks are being submitted as a full and complete response to the Official Action dated July 1, 2003. In view of the above amendments and the following remarks, the Examiner is respectfully requested to give due reconsideration to this application, in connection with the Request for Continued Examination filed herewith, to indicate the allowability of the claims, and to pass this case to issue.

Status of the Claims

Claims 1-15 are under consideration in this application. Claims 1-6, 8-13 are being amended, as set forth in the above marked-up presentation of the claim amendments, in order to more particularly define and distinctly claim applicants' invention. New claims 14-15 are being added to recite other embodiments described in the specification.

Additional Amendments

The specification and the claims are being amended to correct formal errors and/or to better recite or describe the features of the present invention as claimed. All the amendments to the claims are supported by the specification. Applicants hereby submit that no new matter is being introduced into the application through the submission of this response.

Formality Rejections

Claims 4, 7, 10-13 were objected as being in improper form because a multiple dependent claim can not depend on another multiple dependent claim. Applicants contend that only claims 12-13 improperly depended on other claims.

Claims 1-7 were rejected under 35 U.S.C. § 101 due to the claiming of the non-statutory subject matter. Applicants contend that the recitation of "thereby grouping biopolymers in the selected subtree into at least one function unit or function group" is being added to each independent claim to a practical application of the invention in the technological art of gene expression analysis. Applicants contend that such recitation in conjunction of the displaying of a selected subtree visually allows one skilled in the art to "*see whether relative genes are assembled in a subtree*" so as to "*determine which function or keyword should be focused on*" (page 5, lines 1-4). This result "*is concrete, tangible and useful. See AT&T, 172 F.3d at 1358,*

50 USPQ2d at 1452" such that the methods/systems as now claimed are statutory process/system claims. MPEP 2106 (IV)(b)(ii) Computer-Related Processes Limited to a Practical Application in the Technological Arts. Accordingly, the withdrawal of the outstanding informality rejection is in order, and is therefore respectfully solicited.

The Abstract was amended into one paragraph. As indicated, the specification and the claims have been amended to correct formal errors and/or to better recite or describe the features of the present invention as claimed. Accordingly, the withdrawal of the outstanding informality rejection is in order, and is therefore respectfully solicited.

Prior Art Rejection

Claims 1-13 were rejected under 35 U.S.C. § 103(a) as being unpatentable over an article by Eisen et al. published in 1998 (hereinafter "Eisen") and in view of an article by Swayne et al. published on Journal of Computational and Graphical Statistics 1998, Vol. 7, No. 1, pp. 1-19 (hereinafter "Swayne"). Claims 1-13 were also rejected being unpatentable over WO 99/09218 assigned to Affymetrix (hereinafter "Affymetrix") in view of U.S. Pat. No. 5,895,474 to Maarek et al. (hereinafter "Maarek"). These rejections have been carefully considered, but are most respectfully traversed, as more fully discussed below.

The method for displaying a dendrogram according to the invention, comprising the steps of: clustering a plurality types of biopolymers based on a set of data obtained by experiments of the plurality types of biopolymers under different conditions, and displaying clustering results thereof in a form of a dendrogram; selecting a **subtree** (defined as "*extending from the selected branch to the downstream leaves*" page 5, lines 14-15) in the dendrogram; and (i) displaying the selected subtree on a separate window (claim 1; Fig. 6; page 8, 1st paragraph), or (ii) replacing the selected subtree with an icon in the dendrogram (claim 3; Fig. 7, page 8, 2nd paragraph), or (iii) in the selected subtree, counting and displaying predetermined keywords and a corresponding number of biopolymers containing in biopolymer information thereof a respective one of the predetermined keywords (claim 5; Figs. 5, 8; page 8, last paragraph), or (iv) designating at least one keyword for the subtree and displaying the subtree and highlighting a location of each biopolymer in the subtree which includes the designated keyword in biopolymer information thereof (claim 6; page 9, 1st paragraph), thereby grouping biopolymers in the selected subtree into at least one function unit or function group.

The invention is also directed to a system for displaying a dendrogram based upon the methods described in claims 1,3, 5-6, as now recited in claim 8-13 and 15.

Applicant respectfully submits that none of the cited prior art references discloses, teaches or suggests such a **subtree-oriented approach in a hierarchical clustering dendrogram**, according to the invention, which can display "*several thousands to ten-thousands of genes*"(page 3, last paragraph) so as to group biopolymers in a selected subtree into at least one function unit or function group.

In contrast, Eisen only teaches a system of cluster analysis for genome-wide expression data, the output of which is displayed as a single tree whose branch length reflecting degree of similarity between the objects. Only one clustering method is selected to computes a dendrogram (rather than applying another clustering method for a subtree) , and images are provided so that one may readily zoom in on the detailed expression patterns of interest to identify the genes that contribute to the expression patterns. All the samples were taken from RNA that was reversed transcribed into cDNA spotted on DNA microarrays. Affymetrix merely provide systems and methods for detecting differences in sample polymers, such as nucleic acid sequences, and hybridization affinity information for the sample polymers is clustered so that the differences, if any, between or among the sample polymers can be readily identified, by clustering the hybridization affinity information of the sample polymers, differences in the sample polymers can be accurately achieved even in the presence of random and systematic errors (Abstract). The sets of hybridization affinity information are clustered and clustering analysis processes typically accept as input multiple patterns of data (e.g., represented by vectors of floating point numbers) and rearrange the patterns into clusters of similar patterns. Preferred embodiments arrange patterns of data into hierarchical clusters where each cluster includes cluster that are more similar to each other than to other clusters (page 10, lines 10-14).

As admitted by the Examiner, Eisen and Affymetrix fail to teach any visualized data manipulation step or mechanism (page 5, 1st paragraph and page 6, lines 13-14 of the outstanding Office Action). In particular, Fig 1 of Eisen and Fig. 9 of Affymetrix (primary references) share the exact same problems as the prior art depicted in Fig. 4 of the specification, i.e., "*when the lengths of these branches are too short relative to the length of the dendrogram, it becomes very difficult to find detailed relationship between the branches of genes as can be appreciated from a range 401in Fig. 4* (page 4, lines 16-20)."

Swayne and Maarek were relied upon by the Examiner to compensate for the deficiencies

of Eisen and Affymetrix respectively. However, Swayne and Maarek do not teach or suggest applying their data visualization systems to any bioploymer expression patterns. Swayne's "XGobi", however, is designed only to provide a general-purpose user interface for manipulating views of data and not specifically intended for displaying and manipulating a dendrogram view, or a subtree of a dendrogram view. The Examiner's reliance upon the "common knowledge and common sense" of one skilled in the art for motivation to apply the teachings in Swayne and Maarek to Eisen and Affymetrix does not fulfill the agency's obligation to cite references to support its conclusions. Instead, the Examiner must provide the specific teaching of allegations of "obviousness" or combination on the record, such as *statements in the prior art,* to allow accountability.

> *To establish a prima facie case of obviousness, the Board must, inter alia, show "some objective teaching in the prior art or that knowledge generally available to one of ordinary skill in the art would lead that individual to combine the relevant teachings of the references." In re Fine, 837 F.2d 1071, 1074, 5 USPQ2d 1596, 1598 (Fed. Cir. 1988). "The motivation, suggestion or teaching may come explicitly from statements in the prior art, the knowledge of one of ordinary skill in the art, or, in some cases the nature of the problem to be solved." Kotzab, 217 F.3d at 1370, 55 USPQ2d at 1317. .... Recently, in In re Lee, 277 F.3d 1338, 61 USPQ2d 1430 (Fed. Cir. 2002), we held that the Board's reliance on "common knowledge and common sense" did not fulfill the agency's obligation to cite references to support its conclusions. Id. at 1344, 61 USPQ2d at 1434. Instead, the Board must document its reasoning on the record to allow accountability. Id. at 1345, 61 USPQ2d at 1435.*
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> See In re Thrift, 298 F.3d 1357.

Such an obligation to provide specific teaching(s) also applies to other existing or future obviousness rejections.

Although the invention visualizes the bioploymer expression patterns into a dendrogram similar to Eisen and Affymetrix, the invention visualizes the data on the subtree level to significantly ease the analysis of an user and to achieve the following unexpected results or properties unknown and non-inherent functions in view of Eisen and Affymetrix or their combinations with Swayne and Maarek, since Eisen and Affymetrix or their combinations do not

inherently achieve the same results. In other words, these advantages would not flow naturally from following the teachings of Eisen and Affymetrix or their combinations, since Eisen and Affymetrix or their combinations fail to suggest any subtree approach in a hierarchical clustering dendrogram.

The presence of the following unexpected properties is evidence of nonobviousness. MPEP§716.02(a). For example, by displaying the selected subtree on a separate window, the invention further allows a user to designate a different clustering method for the biopolymers included in the subtree displayed on the separate window, and secondarily clustering the biopolymers included in the subtree according to the designated clustering method, and displaying secondarily clustering results thereof in a form of a dendrogram (Fig. 6; page 8, 1st paragraph). As another example, by replacing the selected subtree with an icon in the dendrogram, the visual presentation of the dendrogram is simplified (Fig. 7, page 8, 2nd paragraph). "*For example, gene groups with similar functions or gene groups with little expression observed can be assembled as a single icon.*" As a third example, in the selected subtree, by counting and displaying predetermined keywords and a corresponding number of biopolymers containing in biopolymer information thereof a respective one of the predetermined keywords ("search for keyword contained in this subtree" Figs. 5, 8; page 8, last paragraph), or designating at least one keyword for the subtree and displaying the subtree and highlighting a location of each biopolymer in the subtree which includes the designated keyword in biopolymer information thereof (page 9, 1st paragraph), "*types of genes assembled in the subtree can readily be known. When the grouping is found to be failed, another grouping algorithm or (dis)similarity can be selected for another clustering. This would aid selection of more appropriate clustering method (page 9, 1st paragraph).*"

> "*Presence of a property not possessed by the prior art is evidence of nonobviousness. In re Papesch, 315 F.2d 381, 137 USPQ 43 (CCPA 1963) (rejection of claims to compound structurally similar to the prior art compound was reversed because claimed compound unexpectedly possessed anti-inflammatory properties not possessed by the prior art compound); Ex parte Thumm, 132 USPQ 66 (Bd. App. 1961) (Appellant showed that the claimed range of ethylene diamine was effective for the purpose of producing " 'regenerated cellulose consisting substantially entirely of skin' " whereas the prior art warned "this compound has 'practically no effect.' ").*

Applicants further contend that the mere fact that one of skill in the art could accidentally apply the references to meet the terms of the claims is not by itself sufficient to support a finding of obviousness. The prior art must provide a motivation or reason for one skilled in the art to provide the unexpected properties without the benefit of appellant's specification, to make the necessary changes in the reference device. *Ex parte Chicago Rawhide Mfg. Co.*, 223 USPQ 351, 353 (Bd. Pat. App. & Inter. 1984). MPEP§2144.04 VI C.

Applicants respectfully caution the Examiner that any reliance on "common knowledge and common sense" to rearrange Eisen and Affymetrix or their combinations to meet the terms of the claims bears the agency's obligation to cite references to support any such modifications. The Examiner must provide the specific teaching of such a modification on the record to allow accountability. See In re Thrift, 298 F.3d 1357.

Contrary to the Examiner's allegation that Swayne's "labeled box" providing information about the magnitude and direction of the contributions of each variable data, allegedly meets the limitation of keywords and icon display as claimed (page 4, lines 26-29; page 6, lines 29-37; page 7, lines 1-2), Swayne does not teach a keyword display related to the biopolymers contained in the subtree as recited in claims 5-6 or an icon substituting a subtree in the dendrogram view as recited in claim 3. Swayne only describes a data visualization system implementing interactive and dynamic methods for manipulating data views, known as "XGobi". Accordingly, the Swayne-Eisen combination does not render obvious the above-mentioned feature of the present invention.

Contrary to the Examiner's allegation that Maarek displays an icon in place of a selected subtree (extending from the selected branch to the downstream leaves; "701" in Fig. 7), Applicant contend that Maarek only displays a square in place of a node (NOT extending from a selected branch to downstream leaves; "32" in Fig. 3). Maarek also fails to teach automatically rescaling and redisplaying a selected subtree and use of keywords contained in subtrees. Maarek only teaches an interactive, tree structured, graphical visualization aid enables a user to better understand and interpret underlying structures in collections of digitally stored data (Abstract). Maarek's visualization aid operates in at least two modes: a first mode in which all branches of the tree depending from the node are displayed as such, and a second mode in which all the information elements to which branches depending from the node lead are indicated as a single list. The system was arranged to respond to predefined user input operation including a node

selection to switch between the first and second modes (col. 2, lines 19-32). The clusters can be "collapsed" such that the dendrogram is cut at a specific internal node to obtain a list of all members of that cluster (col. 2, lines 48-50; col. 6, lines 22-32). Each node may be pictured as a square representing a cluster (col. 2, lines 56-64).

Applicants contend that cited prior references and their combinations fail to teach or disclose each and every feature of the present invention as disclosed in independent claims 1, 3, 5-6 and 8. As such, the present invention as now claimed is distinguishable and thereby allowable over the rejections raised in the Office Action. The withdrawal of the outstanding prior art rejections is in order, and is respectfully solicited.

In view of all the above, clear and distinct differences as discussed exist between the present invention as now claimed and the prior art reference upon which the rejections in the Office Action rely, Applicant respectfully contends that the prior art references cannot anticipate the present invention or render the present invention obvious. Rather, the present invention as a whole is distinguishable, and thereby allowable over the prior art.

Favorable reconsideration of this application is respectfully solicited. Should there be any outstanding issues requiring discussion that would further the prosecution and allowance of the above-captioned application, the Examiner is invited to contact the Applicant's undersigned representative at the address and phone number indicated below.

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November 24, 2003

SPF/JCM/JT